REMARKS

This Response, filed in reply to the Office Action dated August 8, 2007, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 1-11 and 15-22 are withdrawn from consideration as being directed to nonelected inventions. Claims 12-14 and 23-29 are rejected. Claims 10, 12 and 14 are currently amended and new Claims 30-33 are introduced. Claims 13 and 23-29 are canceled. Entry of these amendments is respectfully requested. Support for the amendments can be found throughout the specification, and at least in the following paragraphs of the published specification.

Support for the amendment to the preamble of Claim 12 can be found at least in paragraph [0038], support for step (1) of Claim 12 can be found at least in paragraphs [0031] and [0096], support for steps (2) and (3) of Claim 12 can be found at least in paragraph [0048], lines 9-11, and support for step (4) of Claim 12 can be found at least in paragraphs [0031], [0041] and [0098], lines 24-26.

Support for the amendment to Claim 14 can be found at least in paragraph [0004] of the published specification and support for new Claims 30-32 can be found at least in paragraph [0004] of the published specification. Support for new Claim 33 can be found at least in Example 5 and Figure 11 of the specification.

Claim 10 has been amended to correct an obvious typographical error. Upon entry of these amendments, Claims 1-12, 14-22 and 30-33 will be all the claims pending in the application.

Drawings

Applicants thank the Examiner for accepting the drawings submitted on February 6, 2006.

Information Disclosure Statements

Applicants thank the Examiner for returning signed and initialed copies of the PTO Forms SB/08 that accompanied the Information Disclosure Statements filed June 27, 2005, and February 6, 2006.

Objection to Claims 24-29 Under 37 CFR 1.75(c)

On page 4 of the Office Action, Claims 24-29 are objected to under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicants respectfully submit that the objection is moot in view of the cancellation of these claims.

Withdrawal of the objection is therefore respectfully requested.

Claim 14 is Enabled Under 35 U.S.C. § 112

On page 5 of the Office Action, Claims 13, 14 and 23-29 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement. The Office alleges that the specification, while being enabling for a screening method for a compound which is capable of enhancing human adiponectin promoter activity, is not enabling for a screening method for a preventive and/or therapeutic medicine for syndromes selected from syndrome X, metabolic syndrome, multiple risk factor syndrome, insulin resistance syndrome, deadly quartet, and visceral fat syndrome.

The Office further alleges that the application fails to demonstrate that an agent capable of altering expression from the promoter construct disclosed in the instant application is capable of treating any of the syndromes recited in the instant claims, or provide any direct evidence that agents identified by the claimed method would be capable of preventing and/or treating

syndrome X, metabolic syndrome, multiple risk factor syndrome, insulin resistance syndrome, deadly quartet, or visceral fat syndrome.

The Office acknowledges that the prior art (i.e. Diez *et al.*, *Eur. J. Endocrinol.*, 2003, 148:293-300) and the instant specification disclose that adiponectin is an adipocyte-derived regulatory factor and a potential therapeutic agent. However, the Office asserts that at the time the instant application was filed, adiponectin had not been established as an effective treatment, or preventative agent, for any condition.

Further, the Office appears to take the position that adiponectin is not a valid biomarker for use as a surrogate endpoint for the treatment of the diseases or conditions recited in the instant claims.

Initially, Applicants point out that Claims 13 and 23-29 have been cancelled, thus the rejection is addressed below as it applies to Claim 14. Applicants traverse the rejection, and submit that Claim 14 is fully enabled in view of the following. Specifically, Applicants respectfully submit that the state of the art at the time of filing demonstrates that activation of adiponectin transcription was an effective approach to treating the diseases recited in Claim 14 as amended. In this regard, Maeda *et al.* (*Nature Medicine*, 2002, 7:731-737), which is described in paragraph [0003] of the published specification, teach that adiponectin, a protein that is abundant in serum, is decreased in obese patients and those having type II diabetes (left column, page 731). Maeda *et al.* also disclose that murine diabetes is improved by treatment with adiponectin (left column, page 731). Further, Maeda *et al.* experimentally demonstrate that insulin resistance is improved upon expression of adiponectin using adiponectin knockout mice (Figure 4).

Further still, Okamoto *et al.* (*Circulation*, 2002, 106:2767-2770), which is also described in paragraph [0003] of the published specification, demonstrates that atherosclerotic foci are decreased when adiponectin is expressed in apolipoprotein E (ApoE)-deficient mice, which

exhibit atheromatous arteriosclerosis (Figure. 1). Applicants respectfully submit that in view of the guidance provided by the instant specification, and the state of the art at the time of filing as evidenced by Maeda *et al.* and Okamoto *et al.*, it would be apparent to one of skill in the art that a compound which increases the expression of adiponectin is useful for the treatment of diabetes, obesity, arteriosclerosis, or insulin resistance syndrome. Further, Applicants respectfully submit that in view of such data, one of skill in the art would realize that Applicants' claimed invention would function predictably as a surrogate endpoint. Accordingly, Applicants submit that Claim 14 is enabled at least in view of the foregoing.

Withdrawal of the rejection is therefore respectfully requested.

Claims 12 and 14 are Not Indefinite Under 35 U.S.C. § 112

On page 11 of the Office Action, Claims 12-14 and 23-29 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The Office alleges that the claims are indefinite in that they recite an outcome of a process, but do not set forth any steps involved in the process.

Applicants hereby amend Claim 12 to recite positive method steps involved in performing the claimed method. Applicants respectfully submit that the amendments to Claim 12 overcome the rejection of Claims 12 and 14. Applicants note that the cancellation of Claims 13 and 23-29 renders moot the rejection of these claims.

Claim 12 has been amended to recite steps (1) through (4), which correspond to reporter expression using DNA containing the native adiponectin promoter sequence (i.e., SEQ ID NO: 1) in the presence or absence of a test compound. Paragraphs [0031] and [0096] of the published specification provide support for transforming a cell with a DNA molecule comprising the nucleotide sequence represented by SEQ ID NO:1 operatively linked to a DNA sequence

encoding a reporter. With regard to the position of SEQ ID NO: 1 and the reporter, support for this limitation can be found in paragraph [0031] of the published specification wherein it is disclosed that "[a] method of connecting a transcriptionally detectable reporter gene to the downstream of the obtained DNA is preferred as a method to examine the promoter activity."

The limitation of transforming an expression plasmid encoding a human PPARγ protein and an expression plasmid encoding a human RXRα protein in Claim 12 finds support in paragraph [0096] of the published specification, where Applicants experimentally demonstrate the transformation of cells with vectors encoding these proteins, individually and in combination, and subsequently measuring reporter expression.

Steps (2) through (4) of Claim 12 find support in paragraph [0098], lines 24-26 of the published specification, wherein the activity of the p(-908)/LUC reporter is analyzed with or without pioglitazone. Support for the term "diluent" in steps (2) and (3) can be found in paragraph [0048], lines 9-11, for example.

Applicants respectfully submit that the amendments to Claim 12 attached herewith overcome the rejection.

Withdrawal of the rejection is therefore respectfully requested.

Claims 12 and 14 are Not Obvious Under 35 U.S.C. § 103(a)

On page 12 of the Office Action, Claims 12-14 and 23-29 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Dufaure-Gare *et al.* (WO 00/26363).

The Office asserts that although Claim 12 recites "consists of", this term is only interpreted as applying to the "promoter region", while the open transition "having" is interpreted as applying to the nucleotide sequence. The Office contends that the claims read on any transformant transformed with a DNA that comprises SEQ ID NO: 1 within a "promoter region."

The Office alleges that on pages 102-103, Dufaure-Gare *et al.* disclose "a method for screening substances or molecules that are able to increase, or ... decrease, the level of expression of the APMI gene [and that] such a method may allow one skilled in the art to select substances exerting a regulating effect on the expression level of the APM1 gene and which may be useful as active ingredients included in pharmaceutical compositions for treating patients suffering from deficiencies in the regulation of expression of the APMI gene, particularly patients suffering from obesity."

Further, the Office alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to practice the screening method of Dufaure-Gare *et al.* using a nucleic acid promoter comprising the entirety of instant SEQ ID NO: 1. The Examiner alleges that Dufaure-Gare *et al.* discloses practicing the method using a sequence comprising nucleotides 1-908 of instant SEQ ID NO: 1, that nucleotides 1-908 of instant SEQ ID NO: 1 are contiguous with nucleotides 909-921 of instant SEQ ID NO: 1, and that nucleotides 1-908 and nucleotides 909-921 can be used together as is found in the native gene.

Applicants traverse the rejection and respectfully submit that the claimed invention is not rendered obvious by Dufaure-Gare *et al.* Applicants point out that Claim 12 as amended mandates that said first and second cells are transformed with a DNA molecule comprising a reporter, an expression plasmid encoding a human PPARγ protein and an expression plasmid encoding a human RXRα protein.

Applicants respectfully submit that Dufaure-Gare *et al.* do not render the instant claims obvious as Dufaure-Gare *et al.* are silent as to any requirement for either PPARγ, RXRα or LRH-1 for the enhancement of adiponectin promoter activity. Dufaure-Gare *et al.* do not even contemplate what regulatory sequences may be present within the adiponectin promoter region, or what transcription factors may be necessary. Accordingly, Dufaure-Gare *et al.* fail to teach an

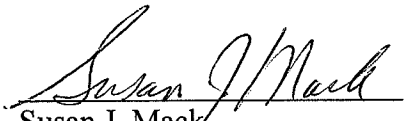
essential limitation of the claims, namely, transformation with an expression plasmid encoding a human PPARγ and an expression plasmid encoding a human RXRα. Accordingly, Dufaure-Gare *et al.* fail to teach each and every limitation of the claims, as is required to maintain a rejection under U.S.C. § 103(a).

Withdrawal of the rejection is therefore respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



Susan J. Mack
Registration No. 30,951

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860
WASHINGTON DC SUGHRUE/265550
65565
CUSTOMER NUMBER

Date: February 8, 2008